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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,743	ELLIOTT, VICKI S.	
	Examiner	Art Unit	
	JON M. LOCKARD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *126-143* is/are pending in the application.

4a) Of the above claim(s) *133-143* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *126-132* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *126-143* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence Alignments*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 126-132, in the reply filed on 21 February 2008 is acknowledged. The traversal is on the ground(s) that the search and examination of Groups I-IV are not unduly burdensome to the Examiner. This is not found persuasive for the following reasons. It is noted this application is a national stage application and therefore U.S. restriction practice (i.e., independent/distinct, undue search burden) does not apply. The inventions of Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, they lack the same or corresponding special technical features for the reasons set forth at pg 2 of the previous Action (mailed 16 October 2007).

2. The restriction requirement is still deemed proper and is therefore made FINAL.

3. Claims 133-143 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 21 February 2008.

Status of Application, Amendments, and/or Claims

4. The response filed on 21 February 2008 has been entered in full. Claims 133-143 are withdrawn from further consideration as discussed *supra*. Therefore, claims 126-143 are pending, and claims 126-133 are the subject of this Office action.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 27 September 2005 has been considered by the examiner.

Claim Rejections - 35 USC § 112, 1st Paragraph (Scope of Enablement)

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 126-133 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for (1) an isolated polypeptide consisting or comprising *the* amino acid sequence SEQ ID NO:1 or (2) an isolated polypeptide encoded by a polynucleotide consisting or comprising *the* nucleic acid sequence SEQ ID NO:2, does not reasonably provide enablement for an isolated polypeptide (1) comprising *an* amino acid sequence of SEQ ID NO:1, or biologically active fragments thereof, or immunogenic fragments thereof; (2) encoded by (a) a polynucleotide comprising *a* polynucleotide sequence of SEQ ID NO:2 or the complement thereof or an RNA equivalent thereof; (b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to SEQ ID NO:2 or the complement thereof or an RNA equivalent thereof; (c) a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that specifically identifies SEQ ID NO:2 or the complement thereof or an RNA equivalent thereof; or (3) an isolated polypeptide produced by culturing a cell transformed with a polynucleotide that is complementary to (a) a polynucleotide comprising a

polynucleotide sequence of SEQ ID NO:2; (b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to SEQ ID NO:2; or (c) a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that specifically identifies SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

8. The specification's disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

9. The claims are drawn quite broadly to an isolated polypeptide (1) comprising *an* amino acid sequence of SEQ ID NO:1, or biologically active fragments thereof, or immunogenic fragments thereof; (2) encoded by (a) a polynucleotide comprising *a* polynucleotide sequence of SEQ ID NO:2 or the complement thereof or an RNA equivalent thereof; (b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to SEQ ID NO:2 or the complement thereof or an RNA equivalent thereof; (c) a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that specifically identifies SEQ ID

NO:2 or the complement thereof or an RNA equivalent thereof; or (3) an isolated polypeptide produced by culturing a cell transformed with a polynucleotide that is complementary to (a) a polynucleotide comprising a polynucleotide sequence of SEQ ID NO:2; (b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to SEQ ID NO:2; or (c) a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that specifically identifies SEQ ID NO:2. It is noted that the recitation "*an* amino acid sequence of SEQ ID NO:1" or "a polynucleotide sequence of SEQ ID NO:2" can be interpreted to mean a partial sequence comprising as few as 2 amino acids or nucleotides, respectively. Thus, the claims have been broadly interpreted by the Examiner as reading upon variants of SEQ ID NOs:1-2, including polypeptides which comprise a subsequence of SEQ ID NO:1 or are encoded by a polynucleotide which comprises a subsequence of SEQ ID NO:2. While the Specification discloses a protein comprising the amino acid sequence SEQ ID NO:1 which is encoded by a polynucleotide that is differentially expressed in lung tumor tissue and fibroblasts isolated from patients with Tangier disease as compared to normal controls (See pg 94, ¶ [0389]-[0390]), it does not teach a commensurate number of the claimed polypeptides. Other than the polypeptide of SEQ ID NO:1, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure has not shown (1) which portions of the protein of SEQ ID NO:1 are critical to the activity of the protein of SEQ ID NO:1 (which itself is not known); (2) what modifications e.g., substitutions, deletions, or additions) one can make to SEQ ID NO:1 that will result in protein mutants or variants with the same function/activity as the protein of SEQ ID NO:1; and (3) any guidance on how to use the variants of SEQ ID NO:1

which would, based on the language of said claims, encompass both active and inactive variants, especially in the absence of any structural or functional limitations in the claims. The state of the art is such that the relationship between the sequence of a protein and its activity is not well understood and unpredictable, and that certain positions in the sequence are critical to the protein's structure/function relationship and can only tolerate only relatively conservative substitutions or no substitutions.

10. The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions and still retain the activity of the protein of SEQ ID NO:1.

11. Although the Specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of the active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, that may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; cited by Applicant).

12. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)

13. Claims 126-132 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

14. Claims 126-132 are drawn quite broadly to an isolated polypeptide (1) comprising *an* amino acid sequence of SEQ ID NO:1, or biologically active fragments thereof, or immunogenic fragments thereof; (2) encoded by (a) a polynucleotide comprising *a* polynucleotide sequence of SEQ ID NO:2 or the complement thereof or an RNA equivalent thereof; (b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to SEQ ID NO:2 or the complement thereof or an RNA equivalent thereof; (c) a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that specifically identifies SEQ ID NO:2 or the complement thereof or an RNA equivalent thereof; or (3) an isolated polypeptide produced by culturing a cell transformed with a polynucleotide that is complementary to (a) a polynucleotide comprising a polynucleotide sequence of SEQ ID NO:2; (b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to SEQ ID NO:2; or (c) a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that specifically identifies SEQ ID NO:2. It is noted that the recitation "*an* amino acid sequence of SEQ ID NO:1" or "a polynucleotide sequence of SEQ ID NO:2" can be interpreted to mean a partial sequence comprising as few as 2 amino acids or nucleotides, respectively. Thus, the claims have been broadly interpreted by the Examiner as reading upon variants of SEQ ID NOs:1-2, including polypeptides which comprise a subsequence of SEQ ID NO:1 or are encoded by a polynucleotide which comprises a subsequence of SEQ ID NO:2. The claims do not require that the polypeptide possess any particular biological activity, nor any particular

conserved structure, or other distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that are defined only by a partial structure.

15. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure. There is not even identification of any particular portion of the structure that must be conserved.

16. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of one polypeptide species (SEQ ID NO:1) and one polynucleotide species (SEQ ID NO:2) is not adequate written description of an entire genus of functionally equivalent polypeptides, which incorporate all fragments, variants, and derivatives encompassed by the claims.

17. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

18. With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

19. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

20. Therefore, only an isolated protein comprising/consisting of *the* amino acid sequence SEQ ID NO:1 or encoded by a polynucleotide comprising/consisting of *the* nucleic acid sequence SEQ ID NO:2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claims 126-131 are rejected under 35 U.S.C. 102(b) as being anticipated by Clark et al. (WO 88/00206, published 14 January 1988).

23. Clark et al. teach an isolated IL-6 polypeptide set forth in Fig. 1 that comprises *an* amino acid sequence of SEQ ID NO:1 and is encoded by a polynucleotide comprising *a* polynucleotide sequence of SEQ ID NO:2 (for example, the polypeptide taught by Clark et al. comprises amino acids 1-90 and 109-163 of SEQ ID NO:1; see attached sequence alignments). Clark et al. also teach recombinant production of said polypeptide (See pg 2). Clark et al. also teach that a preferred embodiment of the IL-6 polypeptide comprises amino acid residues 28-212 of Fig. 1, which, given the broadest reasonable interpretation, would be considered a biologically active fragment. This fragment would also be immunogenic, absent any evidence to the contrary. Moreover, given the high degree of percent identity between the IL-6 polypeptide taught by Clark et al. and polypeptide of SEQ ID NO:1 of the instant application, the polynucleotide encoding the IL-6 polypeptide taught by Clark et al. would inherently comprise *a* polynucleotide sequence of SEQ ID NO:2, comprise *a* naturally occurring polynucleotide sequence of SEQ ID NO:2 at least 90% identical to SEQ ID NO:2, and comprise *a portion* of the polynucleotide sequence of SEQ ID NO:2 that would specifically identify SEQ ID NO:2. It is noted that

specifically has not been interpreted as the equivalent of uniquely. Furthermore, as previously noted, the recitation "*an* amino acid sequence of SEQ ID NO:1" or "a polynucleotide sequence of SEQ ID NO:2" can be interpreted to mean a partial sequence comprising as few as 2 amino acids or nucleotides, respectively. Thus, the claims have been broadly interpreted by the Examiner as reading upon variants of SEQ ID NOs:1-2, including polypeptides which comprise a subsequence of SEQ ID NO:1 or are encoded by a polynucleotide which comprises a subsequence of SEQ ID NO:2. Thus, the Clark et al. reference meets all the limitations of claims 126-131.

Summary

24. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Manjunath N. Rao, Ph.D.**, can be reached on **(571) 272-0939**. The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jon M. Lockard, Ph.D.
May 12, 2008

/Jon M Lockard/
Examiner, Art Unit 1647